

wherein

R is hydrogen or methyl,

R<sup>1</sup> is hydrogen, halogen, hydroxy, benzyloxy, amino or hydroxymethyl,

R<sup>2</sup> is hydrogen, hydroxymethyl, -NHR<sup>3</sup>, -SO<sub>2</sub>NR<sup>4</sup>R<sup>4'</sup> or nitro,

R<sup>3</sup> is hydrogen, methyl, -SO<sub>2</sub>R<sup>5</sup>, formyl or -CONHR<sup>6'</sup>,

R<sup>4</sup> and R<sup>4'</sup> are independently hydrogen, lower alkyl or benzyl,

R<sup>5</sup> is lower alkyl, benzyl or -NR<sup>4</sup>R<sup>4'</sup>,

R<sup>6</sup> is hydrogen or lower alkyl,

R<sup>6'</sup> is hydrogen or lower alkyl,

R<sup>9</sup> is hydrogen, amino, acetylamino or hydroxy, and

X is N, O, S or methylene;

provided that when X is N, O or S,

then R<sup>9</sup> is hydrogen, either R<sup>7</sup> or R<sup>8</sup> is hydrogen, and the other is hydrogen, amino, acetylamino or hydroxy; and

provided that when X is methylene,

then both R<sup>7</sup> and R<sup>8</sup> are hydrogen

wherein said packaging material comprises a label or a written material which indicates that [the compound defined in Claim 10] said compound can or should be used for preventing and/or treating dysuria.--

#### **REMARKS**

A Notice of Allowance has been received in the above-identified application, but the issue fee has not, as yet, been paid.

Minor editorial errors have been corrected in Claim 10. Specifically, in the definition of compound (a) substituent R<sup>1</sup>, the spelling of the term "arylalkyl" has been corrected; in the definition of compound (b), substituent R<sup>1</sup> at (16) the term "C<sub>1</sub>-C<sub>10</sub>" has replaced by "C<sub>1</sub>-C<sub>10</sub>" and for X at (2) the term -CH<sub>2</sub>- corrected to --CH<sub>2</sub>-CH<sub>2</sub>- (see the specification, page 34, line 16).

The amendments to dependent Claims 17-20 are lengthy, however, these claims have merely been redrafted in independent form by replacing "as defined by Claim 10" with the actual description of the compounds described by Claim 10. Accordingly, the Applicants do not believe that any new matter has been introduced.

In view of the nature of the errors no new search is required.

A check in the amount of \$252.00 is attached to cover fees for converting dependent Claims 17-20 to independent claims. Please charge any additional fees for the papers being

filed herewith and for which no check is enclosed herewith, or credit any overpayment to deposit Account 15-0030.

Information Disclosure Statement

The Applicants respectfully request that the Examiner acknowledge consideration of the documents cited on the Information Disclosure Statement (IDS) filed February 14, 2002. For the convenience of the Examiner a copy of Form 1449 from this IDS is attached to this response.

Foreign Priority

The Applicants respectfully request that the Examiner provide written acknowledgement that foreign priority documents Australia, PP2826, filed April 6, 1998 and Australia PP5058, filed August 4, 1998 have been received in U.S. Application 09/646,878. Applicants also request that the Examiner correct the indication that a claim for domestic priority under 35 U.S.C. 119(e) (to a provisional application) had been made.

Respectfully submitted,

OBLON, SPIVAK, McCLELLAND,  
MAIER & NEUSTADT, P.C.

COPY

Norman F. Oblon  
Attorney of Record  
Registration No.: 24,618



22850

Thomas M. Cunningham  
Registration No.: 45,394

PHONE NO.: (703) 413-3000  
FAX NO.: (703) 413-2220  
NFO:TMC:krs  
I:\atty\Tmc\2003-06\219501-Amend312.wpd

COPY

**MARKED UP COPY OF AMENDMENT**

--10. (Twice amended) A method for the prophylactic and/or therapeutic treatment of dysuria that comprises:

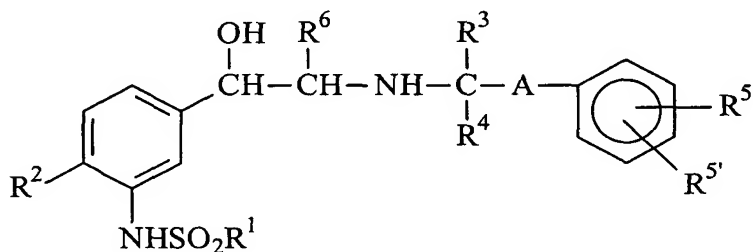
administering to a human being or an animal an effective amount of a compound, which is a  $\beta_3$  adrenergic receptor agonist, having a general formula selected from the group consisting of formula (IV), (V), (VI), (VII) and (VIII),

or a salt or prodrug thereof, or for the compound of formula (VII) an ester or amide thereof;

wherein

(a) a compound of formula (IV) is represented by the following general formula:

wherein

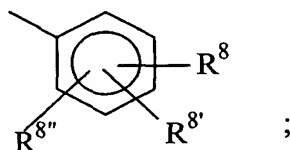


(IV)

$R^1$  is lower alkyl, aryl or [arylakyl] arylalkyl;

$R^2$  is hydrogen, hydroxy, alkoxy,  $-CH_2OH$ , cyano,  $-C(O)OR^7$ ,  $-CO_2H$ ,  $-CONH_2$ , tetrazole,  $-CH_2NH_2$  or halogen;

$R^3$  is hydrogen, alkyl, heterocycle or



$R^4$  is hydrogen, alkyl or B;

$R^5$ ,  $R^{5'}$ ,  $R^8$ ,  $R^{8'}$  and  $R^{8''}$  are independently hydrogen, alkoxy, lower alkyl, halogen,  $-OH$ ,  $-CN$ ,  $-(CH_2)_nNR^6COR^7$ ,  $-CON(R^6)R^{6'}$ ,  $-CON(R^6)OR^{6'}$ ,  $-CO_2R^6$ ,  $-SR^7$ ,  $-SOR^7$ ,  $-SO_2R^7$ ,

copy

$-N(R^6)SO_2R^1$ ,  $-N(R^6)R^{6'}$ ,  $-NR^6COR^7$ ,  $-OCH_2CON(R^6)R^{6'}$ ,  $-OCH_2CO_2R^7$  or aryl; or

$R^5$  and  $R^{5'}$  or  $R^8$  and  $R^{8'}$  may together with the carbon atoms to which they are attached form an aryl or heterocycle;

$R^6$  and  $R^{6'}$  are independently hydrogen or lower alkyl; and

$R^7$  is lower alkyl;

$R^9$  and  $R^{9'}$  are independently hydrogen, lower alkyl, alkyl, cycloalkyl, arylalkyl, aryl, heteroaryl; or

$R^9$  and  $R^{9'}$  may together with the nitrogen atom to which they are attached form a heterocycle;

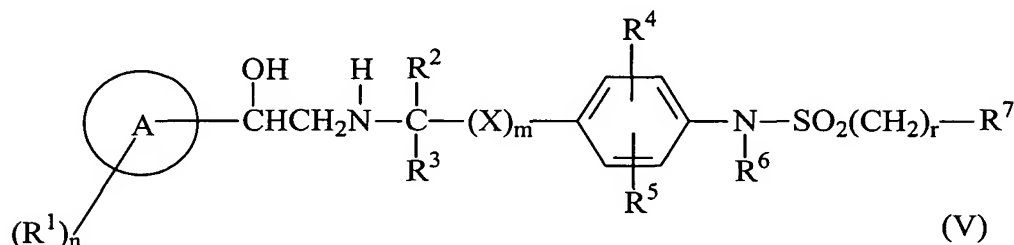
A is a bond,  $-(CH_2)_n-$  or  $-CH(B)-$ , wherein n is an integer of 1, 2 or 3 and

B is  $-CN$ ,  $-CON(R^9)R^{9'}$  or  $-CO_2R^7$ ;

with the proviso that when A is a bond or  $-(CH_2)_n-$  and  $R^3$  is hydrogen or unsubstituted alkyl, then  $R^4$  is B or substituted alkyl;

(b) a compound of formula (V) is represented by the following general formula:

wherein



n is 0 to 5;

m is 0 or 1;

r is 0 to 3;

A is pyridinyl;

$R^1$  is (1) hydroxy, (2) oxo, (3) halogen, (4) cyano, (5)  $NR^8R^8$ , (6)  $SR^8$ , (7) trifluoromethyl, (8)  $C_1-C_{10}$  alkyl, (9)  $OR^8$ , (10)  $SO_2R^9$ , (11)  $OCOR^9$ , (12)  $NR^8COR^9$ , (13)  $COR^9$ , (14)  $NR^8SO_2R^9$ , (15)  $NR^8CO_2R^8$ , or (16)  $[C_1-C_{10}]$   $C_1-C_{10}$  alkyl substituted by hydroxy, halogen, cyano,  $NR^8R^8$ ,  $SR^8$ , trifluoromethyl,  $OR^8$ ,  $C_3-C_8$  cycloalkyl, phenyl,  $NR^8COR^9$ ,  $COR^9$ ,  $SO_2R^9$ ,  $OCOR^9$ ,  $NR^8SO_2R^9$  or  $NR^8CO_2R^8$ ;

$R^2$  and  $R^3$  are independently (1) hydrogen, (2)  $C_1-C_{10}$  alkyl or (3)  $C_1-C_{10}$  alkyl with 1 to 4 substituents selected from hydroxy,  $C_1-C_{10}$  alkoxy, or halogen;

X is (1)  $-\text{CH}_2-$ , (2)  $-\text{CH}_2-\text{CH}_2-$ , (3)  $-\text{CH}=\text{CH}-$  or (4)  $-\text{CH}_2\text{O}-$ ;

$\text{R}^4$  and  $\text{R}^5$  are independently (1) hydrogen, (2)  $\text{C}_1\text{-C}_{10}$  alkyl, (3) halogen, (4)  $\text{NHR}^8$ , (5)  $\text{OR}^8$ , (6)  $\text{SO}_2\text{R}^9$  or (7)  $\text{NHSO}_2\text{R}^9$ ;

$\text{R}^6$  is (1) hydrogen or (2)  $\text{C}_1\text{-C}_{10}$  alkyl;

$\text{R}^7$  is  $\text{Z}-(\text{R}^{1a})_n$ ;

$\text{R}^{1a}$  is (1)  $\text{R}^1$ , (2)  $\text{C}_3\text{-C}_8$  cycloalkyl, (3) phenyl optionally substituted with up to 4 groups independently selected from  $\text{R}^8$ ,  $\text{NR}^8\text{R}^8$ ,  $\text{OR}^8$ ,  $\text{SR}^8$  or halogen, or (4) 5 or 6-membered heterocycle with from 1 to 4 heteroatoms selected from oxygen, sulfur or nitrogen, optionally substituted with up to four groups independently selected from oxo,  $\text{R}^8$ ,  $\text{NR}^8\text{R}^8$ ,  $\text{OR}^8$ ,  $\text{SR}^8$ , or halogen;

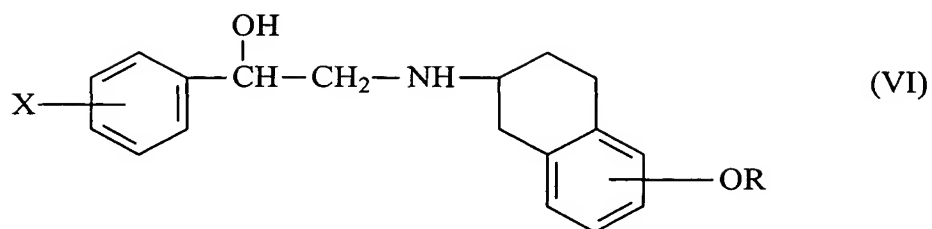
Z is (1) phenyl, (2) naphthyl, (3) or a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur or nitrogen, (4) a benzene ring fused to a  $\text{C}_3\text{-C}_8$  cycloalkyl ring, (5) a benzene ring fused to a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur or nitrogen, (6) a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur or nitrogen fused to a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur or nitrogen, or (7) a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur or nitrogen fused to a  $\text{C}_3\text{-C}_8$  cycloalkyl ring;

$\text{R}^8$  is (1) hydrogen, (2)  $\text{C}_1\text{-C}_{10}$  alkyl, (3)  $\text{C}_3\text{-C}_8$  cycloalkyl, (4) Z optionally having 1 to 4 substituents selected from halogen, nitro, oxo,  $\text{NR}^{10}\text{R}^{10}$ ,  $\text{C}_1\text{-C}_{10}$  alkyl,  $\text{C}_1\text{-C}_{10}$  alkoxy,  $\text{C}_1\text{-C}_{10}$  alkylthio, and  $\text{C}_1\text{-C}_{10}$  alkyl having 1 to 4 substituents selected from hydroxy, halogen,  $\text{CO}_2\text{H}$ ,  $\text{CO}_2\text{-C}_1\text{-C}_{10}$  alkyl,  $\text{SO}_2\text{-C}_1\text{-C}_{10}$  alkyl,  $\text{C}_3\text{-C}_8$  cycloalkyl,  $\text{C}_1\text{-C}_{10}$  alkoxy, or Z optionally substituted by from 1 to 3 halogen,  $\text{C}_1\text{-C}_{10}$  alkyl or  $\text{C}_1\text{-C}_{10}$  alkoxy, or (5)  $\text{C}_1\text{-C}_{10}$  alkyl having 1 to 4 substituents selected from hydroxy, halogen,  $\text{CO}_2\text{H}$ ,  $\text{CO}_2\text{-C}_1\text{-C}_{10}$  alkyl,  $\text{SO}_2\text{-C}_1\text{-C}_{10}$  alkyl,  $\text{C}_3\text{-C}_8$  cycloalkyl,  $\text{C}_1\text{-C}_{10}$  alkoxy,  $\text{C}_1\text{-C}_{10}$  alkyl, or Z optionally substituted by from 1 to 4 halogen,  $\text{C}_1\text{-C}_{10}$  alkyl or  $\text{C}_1\text{-C}_{10}$  alkoxy;

$\text{R}^9$  is (1)  $\text{R}^8$  or (2)  $\text{NR}^8\text{R}^8$ ; and

$\text{R}^{10}$  is (1)  $\text{C}_1\text{-C}_{10}$  alkyl, or (2) two  $\text{R}^{10}$  groups together with the N to which they are attached forming a 5 or 6-membered ring optionally substituted with  $\text{C}_1\text{-C}_{10}$  alkyl;

(c) a compound of formula (VI) is:

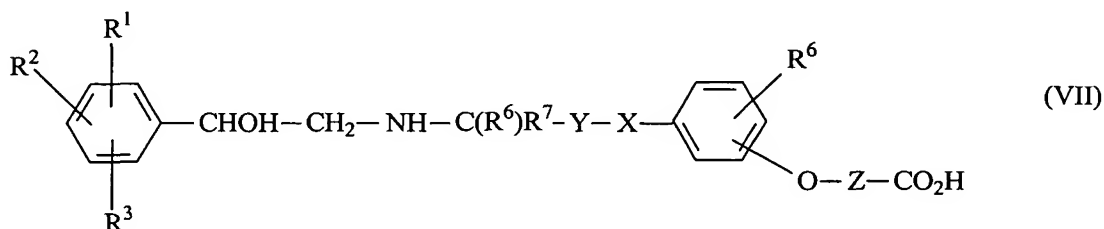


wherein

X is hydrogen, halogen, trifluoromethyl or lower alkyl, and

R is hydrogen; lower alkyl which may have a suitable substituent selected from the group consisting of cyclo(C<sub>3</sub>-C<sub>7</sub>)alkyl, hydroxy, lower alkoxy, carboxy and lower alkoxycarbonyl; cyclo(C<sub>3</sub>-C<sub>7</sub>)alkyl or lower alkanoyl;

(d) a compound of formula (VII) is represented by the following general formula:



wherein

R<sup>1</sup> is a hydrogen, fluorine, chlorine or bromine atom or a hydroxyl, hydroxymethyl, methyl, methoxyl, amino, formamido, acetamido, methylsulphonylamido, nitro, benzyloxy, methylsulphonylmethyl, ureido, trifluoromethyl or p-methoxybenzylamino group;

R<sup>2</sup> is a hydrogen, fluorine, chlorine or bromine atom or a hydroxyl group;

R<sup>3</sup> is a hydrogen, chlorine or bromine atom or a hydroxyl group,

R<sup>4</sup> is a hydrogen atom or a methyl group;

R<sup>5</sup> is a hydrogen atom or a methyl group;

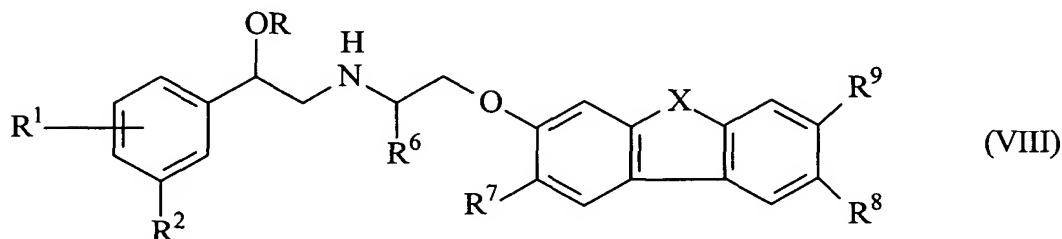
R<sup>6</sup> is a hydrogen, fluorine or chlorine atom or a methyl, methoxyl or hydroxy group;

X is an oxygen atom or a bond;

Y is an alkylene group of up to 6 carbon atoms or a bond; and

Z is an alkylene, alkenylene or alkynylene group of up to 10 carbon atoms; and

(e) a compound of formula (VIII) is represented by the following general formula:



wherein

R is hydrogen or methyl,

R<sup>1</sup> is hydrogen, halogen, hydroxy, benzyloxy, amino or hydroxymethyl,

R<sup>2</sup> is hydrogen, hydroxymethyl, -NHR<sup>3</sup>, -SO<sub>2</sub>NR<sup>4</sup>R<sup>4'</sup> or nitro,

R<sup>3</sup> is hydrogen, methyl, -SO<sub>2</sub>R<sup>5</sup>, formyl or -CONHR<sup>6</sup>,

R<sup>4</sup> and R<sup>4'</sup> are independently hydrogen, lower alkyl or benzyl,

R<sup>5</sup> is lower alkyl, benzyl or -NR<sup>4</sup>R<sup>4'</sup>,

R<sup>6</sup> is hydrogen or lower alkyl,

R<sup>6'</sup> is hydrogen or lower alkyl,

R<sup>9</sup> is hydrogen, amino, acetylamino or hydroxy, and

X is N, O, S or methylene;

provided that when X is N, O or S,

then R<sup>9</sup> is hydrogen, either R<sup>7</sup> or R<sup>8</sup> is hydrogen, and the other is hydrogen, amino, acetylamino or hydroxy; and

provided that when X is methylene,

then both R<sup>7</sup> and R<sup>8</sup> are hydrogen.

--17. (Twice amended) A method for the prophylactic and/or the therapeutic treatment of pollakiuria or urinary incontinence comprising administering to a subject in need thereof an effective amount of

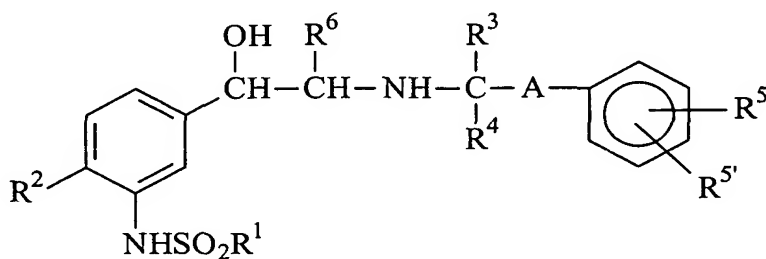
[the compound as defined in Claim 10 or a pharmaceutically acceptable salt thereof]  
a compound, which is a  $\beta_3$  adrenergic receptor agonist, having a general formula selected from the group consisting of formula (IV), (V), (VI), (VII) and (VIII),  
or a salt or prodrug thereof, or for the compound of formula (VII) an ester or amide

thereof;

wherein

(a) a compound of formula (IV) is represented by the following general formula:

wherein

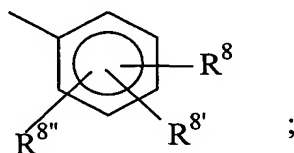


(IV)

$\text{R}^1$  is lower alkyl, aryl or arylalkyl;

$\text{R}^2$  is hydrogen, hydroxy, alkoxy,  $-\text{CH}_2\text{OH}$ , cyano,  $-\text{C}(\text{O})\text{OR}^7$ ,  $-\text{CO}_2\text{H}$ ,  $-\text{CONH}_2$ , tetrazole,  $-\text{CH}_2\text{NH}_2$  or halogen;

$\text{R}^3$  is hydrogen, alkyl, heterocycle or



$\text{R}^4$  is hydrogen, alkyl or B;

$\text{R}^5$ ,  $\text{R}^{5'}$ ,  $\text{R}^8$ ,  $\text{R}^{8'}$  and  $\text{R}^{8''}$  are independently hydrogen, alkoxy, lower alkyl, halogen,  $-\text{OH}$ ,  $-\text{CN}$ ,  $-(\text{CH}_2)_n\text{NR}^6\text{COR}^7$ ,  $-\text{CON}(\text{R}^6)\text{R}^{6'}$ ,  $-\text{CON}(\text{R}^6)\text{OR}^{6'}$ ,  $-\text{CO}_2\text{R}^6$ ,  $-\text{SR}^7$ ,  $-\text{SOR}^7$ ,  $-\text{SO}_2\text{R}^7$ ,  $-\text{N}(\text{R}^6)\text{SO}_2\text{R}^1$ ,  $-\text{N}(\text{R}^6)\text{R}^{6'}$ ,  $-\text{NR}^6\text{COR}^7$ ,  $-\text{OCH}_2\text{CON}(\text{R}^6)\text{R}^{6'}$ ,  $-\text{OCH}_2\text{CO}_2\text{R}^7$  or aryl; or

$\text{R}^5$  and  $\text{R}^{5'}$  or  $\text{R}^8$  and  $\text{R}^{8'}$  may together with the carbon atoms to which they are attached form an aryl or heterocycle;

$\text{R}^6$  and  $\text{R}^{6'}$  are independently hydrogen or lower alkyl; and

$\text{R}^7$  is lower alkyl;

$\text{R}^9$  and  $\text{R}^{9'}$  are independently hydrogen, lower alkyl, alkyl, cycloalkyl, arylalkyl, aryl, heteroaryl; or

$\text{R}^9$  and  $\text{R}^{9'}$  may together with the nitrogen atom to which they are attached form a heterocycle;

A is a bond,  $-(\text{CH}_2)_n-$  or  $-\text{CH}(\text{B})-$ , wherein n is an integer of 1, 2 or 3 and

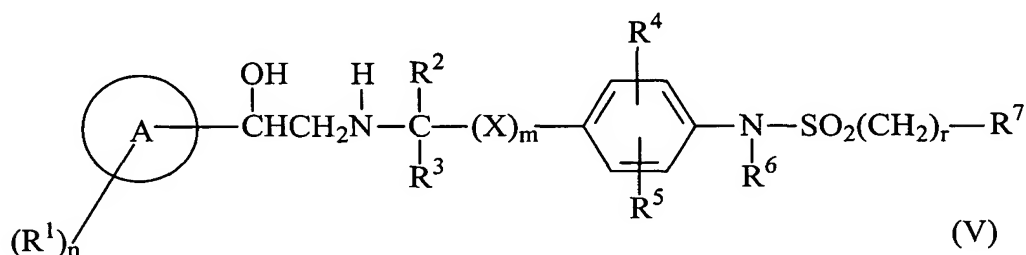


B is -CN, -CON(R<sup>9</sup>)R<sup>9a</sup>- or -CO<sub>2</sub>R<sup>7</sup>;

with the proviso that when A is a bond or -(CH<sub>2</sub>)<sub>n</sub>- and R<sup>3</sup> is hydrogen or unsubstituted alkyl, then R<sup>4</sup> is B or substituted alkyl;

(b) a compound of formula (V) is represented by the following general formula:

wherein



n is 0 to 5;

m is 0 or 1;

r is 0 to 3;

A is pyridinyl;

R<sup>1</sup> is (1) hydroxy, (2) oxo, (3) halogen, (4) cyano, (5) NR<sup>8</sup>R<sup>8</sup>, (6) SR<sup>8</sup>, (7) trifluoromethyl, (8) C<sub>1</sub>-C<sub>10</sub> alkyl, (9) OR<sup>8</sup>, (10) SO<sub>2</sub>R<sup>9</sup>, (11) OCOR<sup>9</sup>, (12) NR<sup>8</sup>COR<sup>9</sup>, (13) COR<sup>9</sup>, (14) NR<sup>8</sup>SO<sub>2</sub>R<sup>9</sup>, (15) NR<sup>8</sup>CO<sub>2</sub>R<sup>8</sup>, or (16) C<sub>1</sub>-C<sub>10</sub> alkyl substituted by hydroxy, halogen, cyano, NR<sup>8</sup>R<sup>8</sup>, SR<sup>8</sup>, trifluoromethyl, OR<sup>8</sup>, C<sub>3</sub>-C<sub>8</sub> cycloalkyl, phenyl, NR<sup>8</sup>COR<sup>9</sup>, COR<sup>9</sup>, SO<sub>2</sub>R<sup>9</sup>, OCOR<sup>9</sup>, NR<sup>8</sup>SO<sub>2</sub>R<sup>9</sup> or NR<sup>8</sup>CO<sub>2</sub>R<sup>8</sup>;

R<sup>2</sup> and R<sup>3</sup> are independently (1) hydrogen, (2) C<sub>1</sub>-C<sub>10</sub> alkyl or (3) C<sub>1</sub>-C<sub>10</sub> alkyl with 1 to 4 substituents selected from hydroxy, C<sub>1</sub>-C<sub>10</sub> alkoxy, or halogen;

X is (1) -CH<sub>2</sub>-, (2) -CH<sub>2</sub>-CH<sub>2</sub>-, (3) -CH=CH- or (4) -CH<sub>2</sub>O-;

R<sup>4</sup> and R<sup>5</sup> are independently (1) hydrogen, (2) C<sub>1</sub>-C<sub>10</sub> alkyl, (3) halogen, (4) NHR<sup>8</sup>, (5) OR<sup>8</sup>, (6) SO<sub>2</sub>R<sup>9</sup> or (7) NHSO<sub>2</sub>R<sup>9</sup>;

R<sup>6</sup> is (1) hydrogen or (2) C<sub>1</sub>-C<sub>10</sub> alkyl;

R<sup>7</sup> is Z-(R<sup>1a</sup>)<sub>n</sub>;

R<sup>1a</sup> is (1) R<sup>1</sup>, (2) C<sub>3</sub>-C<sub>8</sub> cycloalkyl, (3) phenyl optionally substituted with up to 4 groups independently selected from R<sup>8</sup>, NR<sup>8</sup>R<sup>8</sup>, OR<sup>8</sup>, SR<sup>8</sup> or halogen, or (4) 5 or 6-membered heterocycle with from 1 to 4 heteroatoms selected from oxygen, sulfur or nitrogen, optionally substituted with up to four groups independently selected from oxo, R<sup>8</sup>, NR<sup>8</sup>R<sup>8</sup>, OR<sup>8</sup>, SR<sup>8</sup>, or halogen;

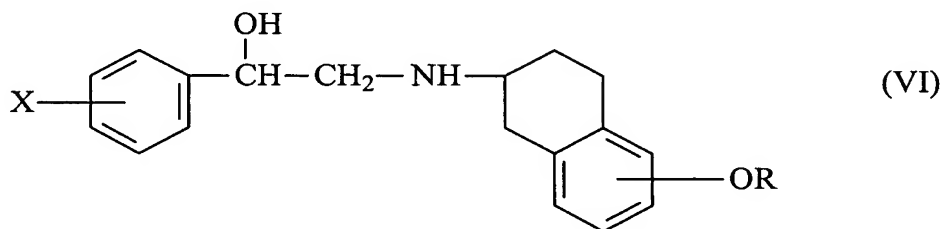
Z is (1) phenyl, (2) naphthyl, (3) or a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur or nitrogen, (4) a benzene ring fused to a C<sub>3</sub>-C<sub>8</sub> cycloalkyl ring, (5) a benzene ring fused to a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur or nitrogen, (6) a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur or nitrogen fused to a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur or nitrogen, or (7) a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur or nitrogen fused to a C<sub>3</sub>-C<sub>8</sub> cycloalkyl ring;

R<sup>8</sup> is (1) hydrogen, (2) C<sub>1</sub>-C<sub>10</sub> alkyl, (3) C<sub>3</sub>-C<sub>8</sub> cycloalkyl, (4) Z optionally having 1 to 4 substituents selected from halogen, nitro, oxo, NR<sup>10</sup>R<sup>10</sup>, C<sub>1</sub>-C<sub>10</sub> alkyl, C<sub>1</sub>-C<sub>10</sub> alkoxy, C<sub>1</sub>-C<sub>10</sub> alkylthio, and C<sub>1</sub>-C<sub>10</sub> alkyl having 1 to 4 substituents selected from hydroxy, halogen, CO<sub>2</sub>H, CO<sub>2</sub>-C<sub>1</sub>-C<sub>10</sub> alkyl, SO<sub>2</sub>-C<sub>1</sub>-C<sub>10</sub> alkyl, C<sub>3</sub>-C<sub>8</sub> cycloalkyl, C<sub>1</sub>-C<sub>10</sub> alkoxy, or Z optionally substituted by from 1 to 3 halogen, C<sub>1</sub>-C<sub>10</sub> alkyl or C<sub>1</sub>-C<sub>10</sub> alkoxy, or (5) C<sub>1</sub>-C<sub>10</sub> alkyl having 1 to 4 substituents selected from hydroxy, halogen, CO<sub>2</sub>H, CO<sub>2</sub>-C<sub>1</sub>-C<sub>10</sub> alkyl, SO<sub>2</sub>-C<sub>1</sub>-C<sub>10</sub> alkyl, C<sub>3</sub>-C<sub>8</sub> cycloalkyl, C<sub>1</sub>-C<sub>10</sub> alkoxy, C<sub>1</sub>-C<sub>10</sub> alkyl, or Z optionally substituted by from 1 to 4 halogen, C<sub>1</sub>-C<sub>10</sub> alkyl or C<sub>1</sub>-C<sub>10</sub> alkoxy;

R<sup>9</sup> is (1) R<sup>8</sup> or (2) NR<sup>8</sup>R<sup>8</sup>; and

R<sup>10</sup> is (1) C<sub>1</sub>-C<sub>10</sub> alkyl, or (2) two R<sup>10</sup> groups together with the N to which they are attached forming a 5 or 6-membered ring optionally substituted with C<sub>1</sub>-C<sub>10</sub> alkyl;

(c) a compound of formula (VI) is:

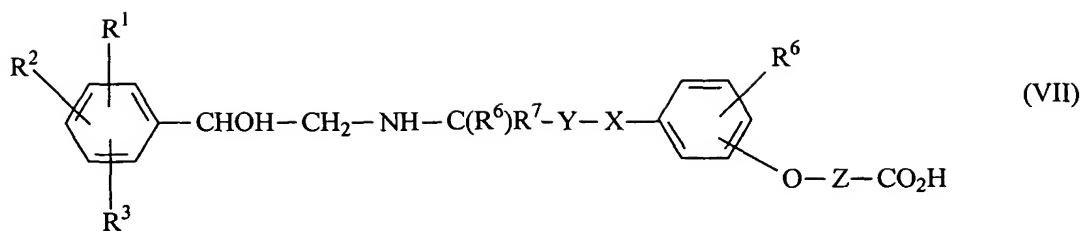


wherein

X is hydrogen, halogen, trifluoromethyl or lower alkyl, and

R is hydrogen; lower alkyl which may have a suitable substituent selected from the group consisting of cyclo(C<sub>3</sub>-C<sub>7</sub>)alkyl, hydroxy, lower alkoxy, carboxy and lower alkoxy carbonyl; cyclo(C<sub>3</sub>-C<sub>7</sub>)alkyl or lower alkanoyl;

(d) a compound of formula (VII) is represented by the following general formula:



wherein

R<sup>1</sup> is a hydrogen, fluorine, chlorine or bromine atom or a hydroxyl, hydroxymethyl, methyl, methoxyl, amino, formamido, acetamido, methylsulphonylamido, nitro, benzyloxy, methylsulphonylmethyl, ureido, trifluoromethyl or p-methoxybenzylamino group;

R<sup>2</sup> is a hydrogen, fluorine, chlorine or bromine atom or a hydroxyl group;

R<sup>3</sup> is a hydrogen, chlorine or bromine atom or a hydroxyl group.

R<sup>4</sup> is a hydrogen atom or a methyl group;

R<sup>5</sup> is a hydrogen atom or a methyl group;

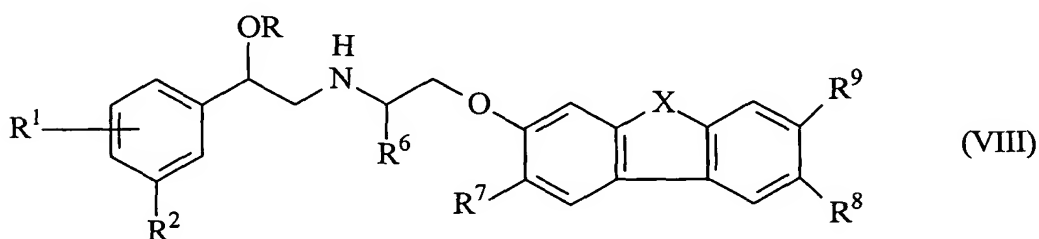
R<sup>6</sup> is a hydrogen, fluorine or chlorine atom or a methyl, methoxyl or hydroxy group;

X is an oxygen atom or a bond;

Y is an alkylene group of up to 6 carbon atoms or a bond; and

Z is an alkylene, alkenylene or alkynylene group of up to 10 carbon atoms; and

(e) a compound of formula (VIII) is represented by the following general formula:



wherein

R is hydrogen or methyl.

R<sup>1</sup> is hydrogen, halogen, hydroxy, benzyloxy, amino or hydroxymethyl.

R<sup>2</sup> is hydrogen, hydroxymethyl, -NHR<sup>3</sup>, -SO<sub>2</sub>NR<sup>4</sup>R<sup>4'</sup> or nitro.

R<sup>3</sup> is hydrogen, methyl, -SO<sub>2</sub>R<sup>5</sup>, formyl or -CONHR<sup>6</sup>.

R<sup>4</sup> and R<sup>4'</sup> are independently hydrogen, lower alkyl or benzyl.

R<sup>5</sup> is lower alkyl, benzyl or -NR<sup>4</sup>R<sup>4'</sup>,

R<sup>6</sup> is hydrogen or lower alkyl,

R<sup>6'</sup> is hydrogen or lower alkyl,

R<sup>9</sup> is hydrogen, amino, acetylamino or hydroxy, and

X is N, O, S or methylene;

provided that when X is N, O or S,

then R<sup>9</sup> is hydrogen, either R<sup>7</sup> or R<sup>8</sup> is hydrogen, and the other is hydrogen, amino, acetylamino or hydroxy; and

provided that when X is methylene,

then both R<sup>7</sup> and R<sup>8</sup> are hydrogen.

18. (Twice amended) A method for the prophylactic and/or the therapeutic treatment of nervous pollakiuria, neurogenic bladder dysfunction, nocturia, unstable bladder, cystospasm, chronic cystitis, chronic prostatitis, overflow incontinence, passive incontinence, reflex incontinence, urge incontinence, urinary stress incontinence comprising administering to a subject in need thereof an effective amount of a compound,

[as defined in Claim 10 or a pharmaceutically acceptable salt thereof]

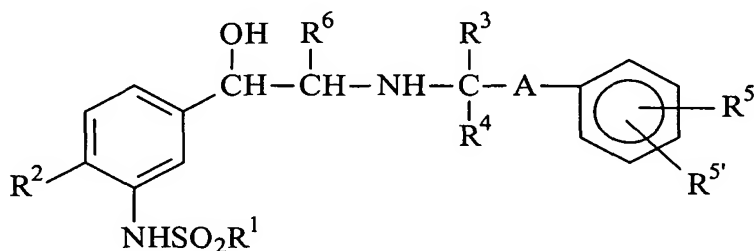
which is a  $\beta_3$  adrenergic receptor agonist, having a general formula selected from the group consisting of formula (IV), (V), (VI), (VII) and (VIII),

or a salt or prodrug thereof, or for the compound of formula (VII) an ester or amide thereof;

wherein

(a) a compound of formula (IV) is represented by the following general formula:

wherein



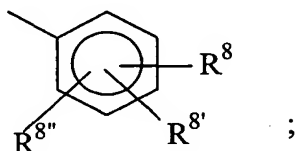
(IV)

R<sup>1</sup> is lower alkyl, aryl or arylalkyl;

R<sup>2</sup> is hydrogen, hydroxy, alkoxy, -CH<sub>2</sub>OH, cyano, -C(O)OR<sup>7</sup>, -CO<sub>2</sub>H, -CONH<sub>2</sub>,

tetrazole, -CH<sub>2</sub>NH<sub>2</sub> or halogen;

R<sup>3</sup> is hydrogen, alkyl, heterocycle or



R<sup>4</sup> is hydrogen, alkyl or B;

R<sup>5</sup>, R<sup>5'</sup>, R<sup>8</sup>, R<sup>8'</sup> and R<sup>8''</sup> are independently hydrogen, alkoxy, lower alkyl, halogen, -OH, -CN, -(CH<sub>2</sub>)<sub>n</sub>NR<sup>6</sup>COR<sup>7</sup>, -CON(R<sup>6</sup>)R<sup>6'</sup>, -CON(R<sup>6</sup>)OR<sup>6'</sup>, -CO<sub>2</sub>R<sup>6</sup>, -SR<sup>7</sup>, -SOR<sup>7</sup>, -SO<sub>2</sub>R<sup>7</sup>, -N(R<sup>6</sup>)SO<sub>2</sub>R<sup>1</sup>, -N(R<sup>6</sup>)R<sup>6'</sup>, -NR<sup>6</sup>COR<sup>7</sup>, -OCH<sub>2</sub>CON(R<sup>6</sup>)R<sup>6'</sup>, -OCH<sub>2</sub>CO<sub>2</sub>R<sup>7</sup> or aryl; or

R<sup>5</sup> and R<sup>5'</sup> or R<sup>8</sup> and R<sup>8'</sup> may together with the carbon atoms to which they are attached form an aryl or heterocycle;

R<sup>6</sup> and R<sup>6'</sup> are independently hydrogen or lower alkyl; and

R<sup>7</sup> is lower alkyl;

R<sup>9</sup> and R<sup>9'</sup> are independently hydrogen, lower alkyl, alkyl, cycloalkyl, arylalkyl, aryl, heteroaryl; or

R<sup>9</sup> and R<sup>9'</sup> may together with the nitrogen atom to which they are attached form a heterocycle;

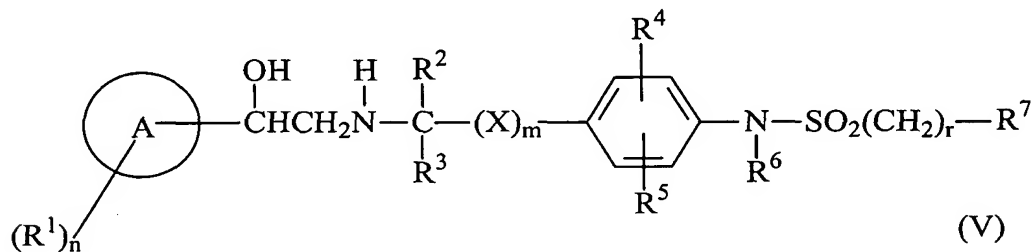
A is a bond, -(CH<sub>2</sub>)<sub>n</sub>- or -CH(B)-, wherein n is an integer of 1, 2 or 3 and

B is -CN, -CON(R<sup>9</sup>)R<sup>9'</sup>- or -CO<sub>2</sub>R<sup>7</sup>;

with the proviso that when A is a bond or -(CH<sub>2</sub>)<sub>n</sub>- and R<sup>3</sup> is hydrogen or unsubstituted alkyl, then R<sup>4</sup> is B or substituted alkyl;

(b) a compound of formula (V) is represented by the following general formula:

wherein



n is 0 to 5;

m is 0 or 1;

r is 0 to 3;

A is pyridinyl;

R<sup>1</sup> is (1) hydroxy, (2) oxo, (3) halogen, (4) cyano, (5) NR<sup>8</sup>R<sup>8</sup>, (6) SR<sup>8</sup>, (7) trifluoromethyl, (8) C<sub>1</sub>-C<sub>10</sub> alkyl, (9) OR<sup>8</sup>, (10) SO<sub>2</sub>R<sup>9</sup>, (11) OCOR<sup>9</sup>, (12) NR<sup>8</sup>COR<sup>9</sup>, (13) COR<sup>9</sup>, (14) NR<sup>8</sup>SO<sub>2</sub>R<sup>9</sup>, (15) NR<sup>8</sup>CO<sub>2</sub>R<sup>8</sup>, or (16) C<sub>1</sub>-C<sub>10</sub> alkyl substituted by hydroxy, halogen, cyano, NR<sup>8</sup>R<sup>8</sup>, SR<sup>8</sup>, trifluoromethyl, OR<sup>8</sup>, C<sub>3</sub>-C<sub>8</sub> cycloalkyl, phenyl, NR<sup>8</sup>COR<sup>9</sup>, COR<sup>9</sup>, SO<sub>2</sub>R<sup>9</sup>, OCOR<sup>9</sup>, NR<sup>8</sup>SO<sub>2</sub>R<sup>9</sup> or NR<sup>8</sup>CO<sub>2</sub>R<sup>8</sup>.

R<sup>2</sup> and R<sup>3</sup> are independently (1) hydrogen, (2) C<sub>1</sub>-C<sub>10</sub> alkyl or (3) C<sub>1</sub>-C<sub>10</sub> alkyl with 1 to 4 substituents selected from hydroxy, C<sub>1</sub>-C<sub>10</sub> alkoxy, or halogen;

X is (1) -CH<sub>2</sub>CH<sub>2</sub>-, (2) -CH<sub>2</sub>-, (3) -CH=CH- or (4) -CH<sub>2</sub>O-;

R<sup>4</sup> and R<sup>5</sup> are independently (1) hydrogen, (2) C<sub>1</sub>-C<sub>10</sub> alkyl, (3) halogen, (4) NHR<sup>8</sup>, (5) OR<sup>8</sup>, (6) SO<sub>2</sub>R<sup>9</sup> or (7) NHSO<sub>2</sub>R<sup>9</sup>;

R<sup>6</sup> is (1) hydrogen or (2) C<sub>1</sub>-C<sub>10</sub> alkyl;

R<sup>7</sup> is Z-(R<sup>1a</sup>)<sub>n</sub>;

R<sup>1a</sup> is (1) R<sup>1</sup>, (2) C<sub>3</sub>-C<sub>8</sub> cycloalkyl, (3) phenyl optionally substituted with up to 4 groups independently selected from R<sup>8</sup>, NR<sup>8</sup>R<sup>8</sup>, OR<sup>8</sup>, SR<sup>8</sup> or halogen, or (4) 5 or 6-membered heterocycle with from 1 to 4 heteroatoms selected from oxygen, sulfur or nitrogen, optionally substituted with up to four groups independently selected from oxo, R<sup>8</sup>, NR<sup>8</sup>R<sup>8</sup>, OR<sup>8</sup>, SR<sup>8</sup>, or halogen;

Z is (1) phenyl, (2) naphthyl, (3) or a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur or nitrogen, (4) a benzene ring fused to a C<sub>3</sub>-C<sub>8</sub> cycloalkyl ring, (5) a benzene ring fused to a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur or nitrogen, (6) a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur or nitrogen fused to a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur or nitrogen, or (7) a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur or nitrogen fused to a C<sub>3</sub>-C<sub>8</sub> cycloalkyl ring;

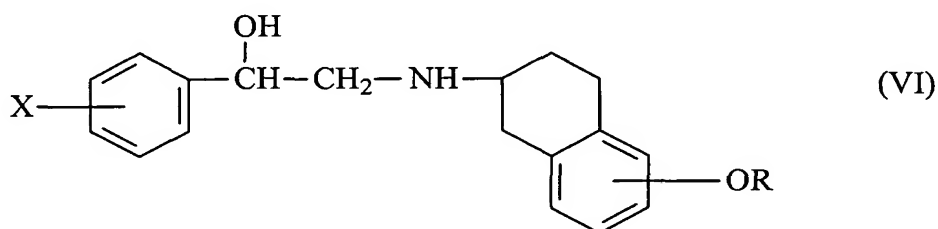
R<sup>8</sup> is (1) hydrogen, (2) C<sub>1</sub>-C<sub>10</sub> alkyl, (3) C<sub>3</sub>-C<sub>8</sub> cycloalkyl, (4) Z optionally having 1 to 4 substituents selected from halogen, nitro, oxo, NR<sup>10</sup>R<sup>10</sup>, C<sub>1</sub>-C<sub>10</sub> alkyl, C<sub>1</sub>-C<sub>10</sub> alkoxy, C<sub>1</sub>-C<sub>10</sub> alkylthio, and C<sub>1</sub>-C<sub>10</sub> alkyl having 1 to 4 substituents selected from hydroxy, halogen, CO<sub>2</sub>H, CO<sub>2</sub>-C<sub>1</sub>-C<sub>10</sub> alkyl, SO<sub>2</sub>-C<sub>1</sub>-C<sub>10</sub> alkyl, C<sub>3</sub>-C<sub>8</sub> cycloalkyl, C<sub>1</sub>-C<sub>10</sub> alkoxy, or Z optionally substituted by from 1 to 3 halogen, C<sub>1</sub>-C<sub>10</sub> alkyl or C<sub>1</sub>-C<sub>10</sub> alkoxy, or (5) C<sub>1</sub>-C<sub>10</sub> alkyl having 1

to 4 substituents selected from hydroxy, halogen,  $\text{CO}_2\text{H}$ ,  $\text{CO}_2\text{-C}_1\text{-C}_{10}$  alkyl,  $\text{SO}_2\text{-C}_1\text{-C}_{10}$  alkyl,  $\text{C}_3\text{-C}_8$  cycloalkyl,  $\text{C}_1\text{-C}_{10}$  alkoxy,  $\text{C}_1\text{-C}_{10}$  alkyl, or Z optionally substituted by from 1 to 4 halogen,  $\text{C}_1\text{-C}_{10}$  alkyl or  $\text{C}_1\text{-C}_{10}$  alkoxy;

$\text{R}^9$  is (1)  $\text{R}^8$  or (2)  $\text{NR}^8\text{R}^8$ ; and

$\text{R}^{10}$  is (1)  $\text{C}_1\text{-C}_{10}$  alkyl, or (2) two  $\text{R}^{10}$  groups together with the N to which they are attached forming a 5 or 6-membered ring optionally substituted with  $\text{C}_1\text{-C}_{10}$  alkyl;

(c) a compound of formula (VI) is:

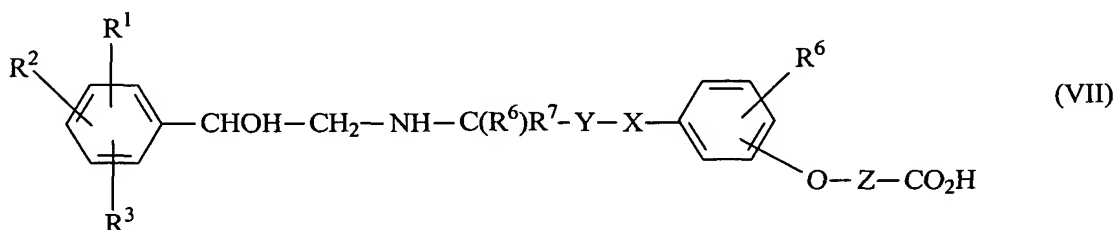


wherein

X is hydrogen, halogen, trifluoromethyl or lower alkyl, and

R is hydrogen; lower alkyl which may have a suitable substituent selected from the group consisting of cyclo( $\text{C}_3\text{-C}_7$ )alkyl, hydroxy, lower alkoxy, carboxy and lower alkoxycarbonyl; cyclo( $\text{C}_3\text{-C}_7$ )alkyl or lower alkanoyl;

(d) a compound of formula (VII) is represented by the following general formula:



wherein

$\text{R}^1$  is a hydrogen, fluorine, chlorine or bromine atom or a hydroxyl, hydroxymethyl, methyl, methoxyl, amino, formamido, acetamido, methylsulphonylamido, nitro, benzyloxy, methylsulphonylmethyl, ureido, trifluoromethyl or p-methoxybenzylamino group;

$\text{R}^2$  is a hydrogen, fluorine, chlorine or bromine atom or a hydroxyl group;

$\text{R}^3$  is a hydrogen, chlorine or bromine atom or a hydroxyl group.

R<sup>4</sup> is a hydrogen atom or a methyl group;

R<sup>5</sup> is a hydrogen atom or a methyl group;

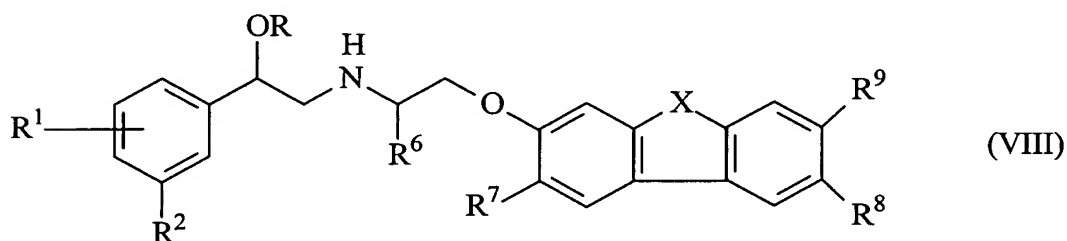
R<sup>6</sup> is a hydrogen, fluorine or chlorine atom or a methyl, methoxyl or hydroxy group;

X is an oxygen atom or a bond;

Y is an alkylene group of up to 6 carbon atoms or a bond; and

Z is an alkylene, alkenylene or alkynylene group of up to 10 carbon atoms; and

(e) a compound of formula (VIII) is represented by the following general formula:



wherein

R is hydrogen or methyl,

R<sup>1</sup> is hydrogen, halogen, hydroxy, benzyloxy, amino or hydroxymethyl,

R<sup>2</sup> is hydrogen, hydroxymethyl, -NHR<sup>3</sup>, -SO<sub>2</sub>NR<sup>4</sup>R<sup>4'</sup> or nitro,

R<sup>3</sup> is hydrogen, methyl, -SO<sub>2</sub>R<sup>5</sup>, formyl or -CONHR<sup>6</sup>,

R<sup>4</sup> and R<sup>4'</sup> are independently hydrogen, lower alkyl or benzyl,

R<sup>5</sup> is lower alkyl, benzyl or -NR<sup>4</sup>R<sup>4'</sup>,

R<sup>6</sup> is hydrogen or lower alkyl,

R<sup>6'</sup> is hydrogen or lower alkyl,

R<sup>9</sup> is hydrogen, amino, acetyl amino or hydroxy, and

X is N, O, S or methylene;

provided that when X is N, O or S,

then R<sup>9</sup> is hydrogen, either R<sup>7</sup> or R<sup>8</sup> is hydrogen, and the other is hydrogen, amino,

acetyl amino or hydroxy; and

provided that when X is methylene,

then both R<sup>7</sup> and R<sup>8</sup> are hydrogen.

--19. (Twice amended) A commercial package comprising:

[the compound as defined in Claim 10]



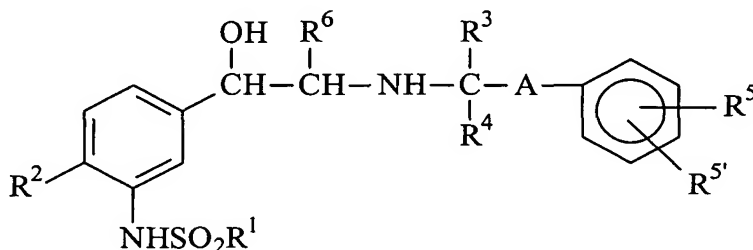
a compound, which is a  $\beta_3$  adrenergic receptor agonist, having a general formula selected from the group consisting of formula (IV), (V), (VI), (VII) and (VIII),

or a salt or prodrug thereof, or for the compound of formula (VII) an ester or amide thereof;

wherein

(a) a compound of formula (IV) is represented by the following general formula:

wherein

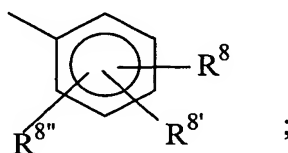


(IV)

$R^1$  is lower alkyl, aryl or arylalkyl;

$R^2$  is hydrogen, hydroxy, alkoxy,  $-\text{CH}_2\text{OH}$ , cyano,  $-\text{C}(\text{O})\text{OR}^7$ ,  $-\text{CO}_2\text{H}$ ,  $-\text{CONH}_2$ , tetrazole,  $-\text{CH}_2\text{NH}_2$  or halogen;

$R^3$  is hydrogen, alkyl, heterocycle or



$R^4$  is hydrogen, alkyl or B;

$R^5$ ,  $R^{5'}$ ,  $R^8$ ,  $R^{8'}$  and  $R^{8''}$  are independently hydrogen, alkoxy, lower alkyl, halogen,  $-\text{OH}$ ,  $-\text{CN}$ ,  $-(\text{CH}_2)_n\text{NR}^6\text{COR}^7$ ,  $-\text{CON}(\text{R}^6)\text{R}^{6'}$ ,  $-\text{CON}(\text{R}^6)\text{OR}^{6'}$ ,  $-\text{CO}_2\text{R}^6$ ,  $-\text{SR}^7$ ,  $-\text{SOR}^7$ ,  $-\text{SO}_2\text{R}^7$ ,  $-\text{N}(\text{R}^6)\text{SO}_2\text{R}^1$ ,  $-\text{N}(\text{R}^6)\text{R}^{6'}$ ,  $-\text{NR}^6\text{COR}^7$ ,  $-\text{OCH}_2\text{CON}(\text{R}^6)\text{R}^{6'}$ ,  $-\text{OCH}_2\text{CO}_2\text{R}^7$  or aryl; or

$R^5$  and  $R^{5'}$  or  $R^8$  and  $R^{8'}$  may together with the carbon atoms to which they are attached form an aryl or heterocycle;

$R^6$  and  $R^{6'}$  are independently hydrogen or lower alkyl; and

$R^7$  is lower alkyl;

$R^9$  and  $R^{9'}$  are independently hydrogen, lower alkyl, alkyl, cycloalkyl, arylalkyl, aryl, heteroaryl; or

R<sup>9</sup> and R<sup>9'</sup> may together with the nitrogen atom to which they are attached form a heterocycle;

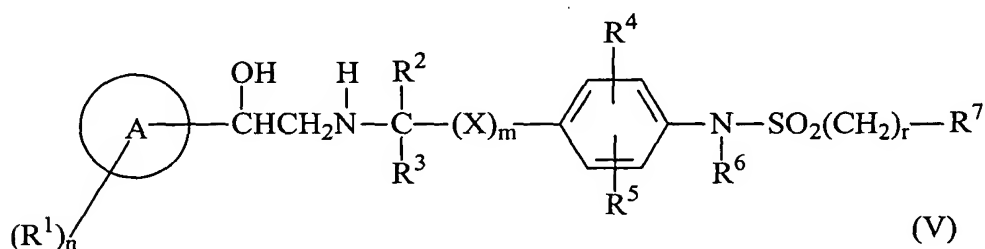
A is a bond, -(CH<sub>2</sub>)<sub>n</sub>- or -CH(B)-, wherein n is an integer of 1, 2 or 3 and

B is -CN, -CON(R<sup>9</sup>)R<sup>9'</sup>- or -CO<sub>2</sub>R<sup>7</sup>;

with the proviso that when A is a bond or -(CH<sub>2</sub>)<sub>n</sub>- and R<sup>3</sup> is hydrogen or unsubstituted alkyl, then R<sup>4</sup> is B or substituted alkyl;

(b) a compound of formula (V) is represented by the following general formula:

wherein



n is 0 to 5;

m is 0 or 1;

r is 0 to 3;

A is pyridinyl;

R<sup>1</sup> is (1) hydroxy, (2) oxo, (3) halogen, (4) cyano, (5) NR<sup>8</sup>R<sup>8</sup>, (6) SR<sup>8</sup>, (7) trifluoromethyl, (8) C<sub>1</sub>-C<sub>10</sub> alkyl, (9) OR<sup>8</sup>, (10) SO<sub>2</sub>R<sup>9</sup>, (11) OCOR<sup>9</sup>, (12) NR<sup>8</sup>COR<sup>9</sup>, (13) COR<sup>9</sup>, (14) NR<sup>8</sup>SO<sub>2</sub>R<sup>9</sup>, (15) NR<sup>8</sup>CO<sub>2</sub>R<sup>8</sup>, or (16) C<sub>1</sub>-C<sub>10</sub> alkyl substituted by hydroxy, halogen, cyano, NR<sup>8</sup>R<sup>8</sup>, SR<sup>8</sup>, trifluoromethyl, OR<sup>8</sup>, C<sub>3</sub>-C<sub>8</sub> cycloalkyl, phenyl, NR<sup>8</sup>COR<sup>9</sup>, COR<sup>9</sup>, SO<sub>2</sub>R<sup>9</sup>, OCOR<sup>9</sup>, NR<sup>8</sup>SO<sub>2</sub>R<sup>9</sup> or NR<sup>8</sup>CO<sub>2</sub>R<sup>8</sup>;

R<sup>2</sup> and R<sup>3</sup> are independently (1) hydrogen, (2) C<sub>1</sub>-C<sub>10</sub> alkyl or (3) C<sub>1</sub>-C<sub>10</sub> alkyl with 1 to 4 substituents selected from hydroxy, C<sub>1</sub>-C<sub>10</sub> alkoxy, or halogen;

X is (1) -CH<sub>2</sub>-, (2) -CH<sub>2</sub>-CH<sub>2</sub>-, (3) -CH=CH- or (4) -CH<sub>2</sub>O-;

R<sup>4</sup> and R<sup>5</sup> are independently (1) hydrogen, (2) C<sub>1</sub>-C<sub>10</sub> alkyl, (3) halogen, (4) NHR<sup>8</sup>, (5) OR<sup>8</sup>, (6) SO<sub>2</sub>R<sup>9</sup> or (7) NHSO<sub>2</sub>R<sup>9</sup>;

R<sup>6</sup> is (1) hydrogen or (2) C<sub>1</sub>-C<sub>10</sub> alkyl;

R<sup>7</sup> is Z-(R<sup>1a</sup>)<sub>n</sub>;

R<sup>1a</sup> is (1) R<sup>1</sup>, (2) C<sub>3</sub>-C<sub>8</sub> cycloalkyl, (3) phenyl optionally substituted with up to 4 groups independently selected from R<sup>8</sup>, NR<sup>8</sup>R<sup>8</sup>, OR<sup>8</sup>, SR<sup>8</sup> or halogen, or (4) 5 or 6-membered

heterocycle with from 1 to 4 heteroatoms selected from oxygen, sulfur or nitrogen, optionally substituted with up to four groups independently selected from oxo,  $R^8$ ,  $NR^8R^8$ ,  $OR^8$ ,  $SR^8$ , or halogen;

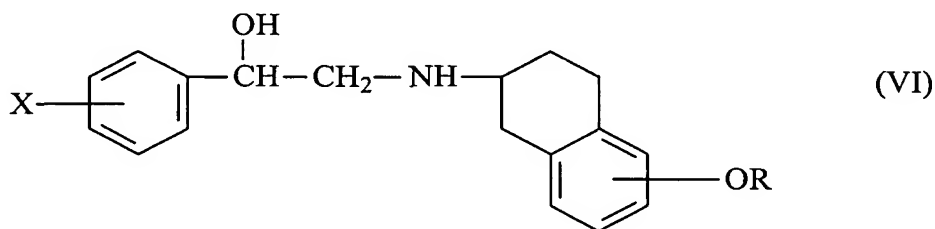
Z is (1) phenyl, (2) naphthyl, (3) or a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur or nitrogen, (4) a benzene ring fused to a  $C_3$ - $C_8$  cycloalkyl ring, (5) a benzene ring fused to a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur or nitrogen, (6) a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur or nitrogen fused to a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur or nitrogen, or (7) a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur or nitrogen fused to a  $C_3$ - $C_8$  cycloalkyl ring;

$R^8$  is (1) hydrogen, (2)  $C_1$ - $C_{10}$  alkyl, (3)  $C_3$ - $C_8$  cycloalkyl, (4) Z optionally having 1 to 4 substituents selected from halogen, nitro, oxo,  $NR^{10}R^{10}$ ,  $C_1$ - $C_{10}$  alkyl,  $C_1$ - $C_{10}$  alkoxy,  $C_1$ - $C_{10}$  alkylthio, and  $C_1$ - $C_{10}$  alkyl having 1 to 4 substituents selected from hydroxy, halogen,  $CO_2H$ ,  $CO_2$ - $C_1$ - $C_{10}$  alkyl,  $SO_2$ - $C_1$ - $C_{10}$  alkyl,  $C_3$ - $C_8$  cycloalkyl,  $C_1$ - $C_{10}$  alkoxy, or Z optionally substituted by from 1 to 3 halogen,  $C_1$ - $C_{10}$  alkyl or  $C_1$ - $C_{10}$  alkoxy, or (5)  $C_1$ - $C_{10}$  alkyl having 1 to 4 substituents selected from hydroxy, halogen,  $CO_2H$ ,  $CO_2$ - $C_1$ - $C_{10}$  alkyl,  $SO_2$ - $C_1$ - $C_{10}$  alkyl,  $C_3$ - $C_8$  cycloalkyl,  $C_1$ - $C_{10}$  alkoxy,  $C_1$ - $C_{10}$  alkyl, or Z optionally substituted by from 1 to 4 halogen,  $C_1$ - $C_{10}$  alkyl or  $C_1$ - $C_{10}$  alkoxy;

$R^9$  is (1)  $R^8$  or (2)  $NR^8R^8$ ; and

$R^{10}$  is (1)  $C_1$ - $C_{10}$  alkyl, or (2) two  $R^{10}$  groups together with the N to which they are attached forming a 5 or 6-membered ring optionally substituted with  $C_1$ - $C_{10}$  alkyl;

(c) a compound of formula (VI) is:



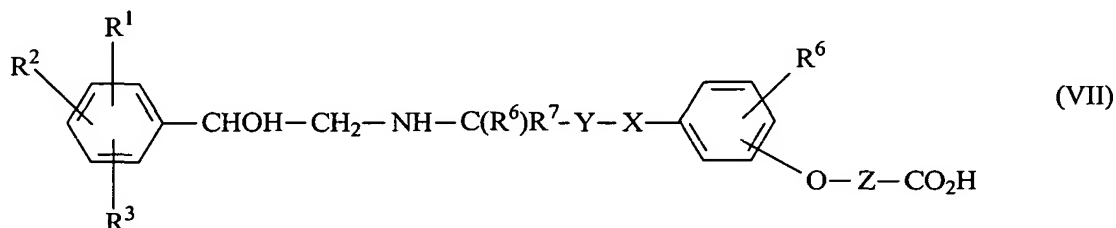
wherein

X is hydrogen, halogen, trifluoromethyl or lower alkyl, and

R is hydrogen; lower alkyl which may have a suitable substituent selected from the

group consisting of cyclo(C<sub>3</sub>-C<sub>7</sub>)alkyl, hydroxy, lower alkoxy, carboxy and lower alkoxycarbonyl; cyclo(C<sub>3</sub>-C<sub>7</sub>)alkyl or lower alkanoyl;

(d) a compound of formula (VII) is represented by the following general formula:



wherein

R<sup>1</sup> is a hydrogen, fluorine, chlorine or bromine atom or a hydroxyl, hydroxymethyl, methyl, methoxyl, amino, formamido, acetamido, methylsulphonylamido, nitro, benzyloxy, methylsulphonylmethyl, ureido, trifluoromethyl or p-methoxybenzylamino group;

R<sup>2</sup> is a hydrogen, fluorine, chlorine or bromine atom or a hydroxyl group;

R<sup>3</sup> is a hydrogen, chlorine or bromine atom or a hydroxyl group,

R<sup>4</sup> is a hydrogen atom or a methyl group;

R<sup>5</sup> is a hydrogen atom or a methyl group;

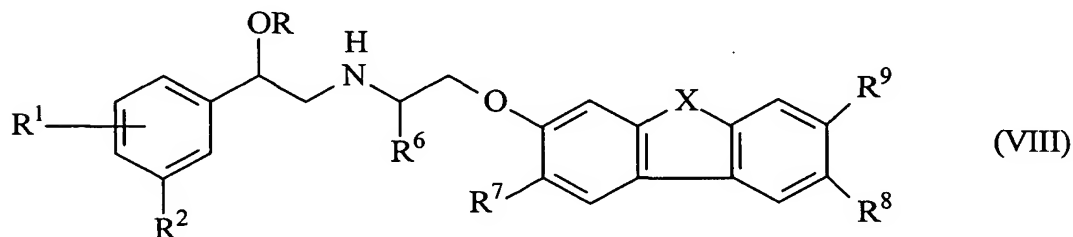
R<sup>6</sup> is a hydrogen, fluorine or chlorine atom or a methyl, methoxyl or hydroxy group;

X is an oxygen atom or a bond;

Y is an alkylene group of up to 6 carbon atoms or a bond; and

Z is an alkylene, alkenylene or alkynylene group of up to 10 carbon atoms; and

(e) a compound of formula (VIII) is represented by the following general formula:



wherein

R is hydrogen or methyl,

R<sup>1</sup> is hydrogen, halogen, hydroxy, benzyloxy, amino or hydroxymethyl,

R<sup>2</sup> is hydrogen, hydroxymethyl, -NHR<sup>3</sup>, -SO<sub>2</sub>NR<sup>4</sup>R<sup>4'</sup> or nitro,

R<sup>3</sup> is hydrogen, methyl, -SO<sub>2</sub>R<sup>5</sup>, formyl or -CONHR<sup>6</sup>,

R<sup>4</sup> and R<sup>4'</sup> are independently hydrogen, lower alkyl or benzyl,

R<sup>5</sup> is lower alkyl, benzyl or -NR<sup>4</sup>R<sup>4'</sup>,

R<sup>6</sup> is hydrogen or lower alkyl,

R<sup>6'</sup> is hydrogen or lower alkyl,

R<sup>9</sup> is hydrogen, amino, acetylamino or hydroxy, and

X is N, O, S or methylene;

provided that when X is N, O or S,

then R<sup>9</sup> is hydrogen, either R<sup>7</sup> or R<sup>8</sup> is hydrogen, and the other is hydrogen, amino, acetylamino or hydroxy; and

provided that when X is methylene,

then both R<sup>7</sup> and R<sup>8</sup> are hydrogen.

and

written matter associated therewith,

wherein the written matter states that the pharmaceutical composition can or should be used for preventing and/or treating dysuria.

20. (Twice amended) An article of manufacture comprising:

a packaging material and

the compound [as defined in Claim 10],

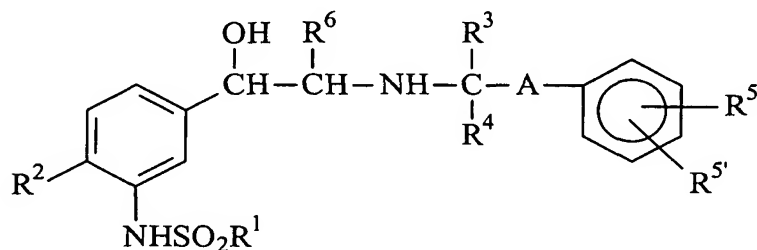
a compound, which is a  $\beta_3$  adrenergic receptor agonist, having a general formula selected from the group consisting of formula (IV), (V), (VI), (VII) and (VIII),

or a salt or prodrug thereof, or for the compound of formula (VII) an ester or amide thereof;

wherein

(a) a compound of formula (IV) is represented by the following general formula:

wherein

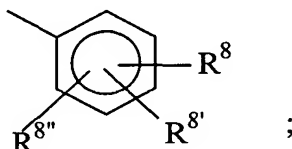


(IV)

R<sup>1</sup> is lower alkyl, aryl or arylalkyl;

R<sup>2</sup> is hydrogen, hydroxy, alkoxy, -CH<sub>2</sub>OH, cyano, -C(O)OR<sup>7</sup>, -CO<sub>2</sub>H, -CONH<sub>2</sub>, tetrazole, -CH<sub>2</sub>NH<sub>2</sub> or halogen;

R<sup>3</sup> is hydrogen, alkyl, heterocycle or



R<sup>4</sup> is hydrogen, alkyl or B;

R<sup>5</sup>, R<sup>5'</sup>, R<sup>8</sup>, R<sup>8'</sup> and R<sup>8''</sup> are independently hydrogen, alkoxy, lower alkyl, halogen, -OH, -CN, -(CH<sub>2</sub>)<sub>n</sub>NR<sup>6</sup>COR<sup>7</sup>, -CON(R<sup>6</sup>)R<sup>6'</sup>, -CON(R<sup>6</sup>)OR<sup>6'</sup>, -CO<sub>2</sub>R<sup>6</sup>, -SR<sup>7</sup>, -SOR<sup>7</sup>, -SO<sub>2</sub>R<sup>7</sup>, -N(R<sup>6</sup>)SO<sub>2</sub>R<sup>1</sup>, -N(R<sup>6</sup>)R<sup>6'</sup>, -NR<sup>6</sup>COR<sup>7</sup>, -OCH<sub>2</sub>CON(R<sup>6</sup>)R<sup>6'</sup>, -OCH<sub>2</sub>CO<sub>2</sub>R<sup>7</sup> or aryl; or

R<sup>5</sup> and R<sup>5'</sup> or R<sup>8</sup> and R<sup>8'</sup> may together with the carbon atoms to which they are attached form an aryl or heterocycle;

R<sup>6</sup> and R<sup>6'</sup> are independently hydrogen or lower alkyl; and

R<sup>7</sup> is lower alkyl;

R<sup>9</sup> and R<sup>9'</sup> are independently hydrogen, lower alkyl, alkyl, cycloalkyl, arylalkyl, aryl, heteroaryl; or

R<sup>9</sup> and R<sup>9'</sup> may together with the nitrogen atom to which they are attached form a heterocycle;

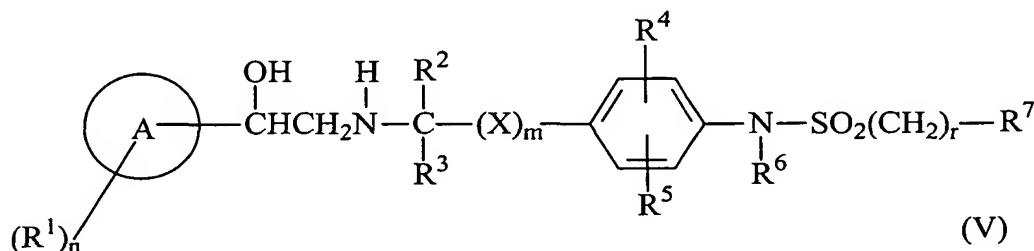
A is a bond, -(CH<sub>2</sub>)<sub>n</sub>- or -CH(B)-, wherein n is an integer of 1, 2 or 3 and

B is -CN, -CON(R<sup>9</sup>)R<sup>9'</sup>- or -CO<sub>2</sub>R<sup>7</sup>;

with the proviso that when A is a bond or -(CH<sub>2</sub>)<sub>n</sub>- and R<sup>3</sup> is hydrogen or unsubstituted alkyl, then R<sup>4</sup> is B or substituted alkyl;

(b) a compound of formula (V) is represented by the following general formula:

wherein



(V)

n is 0 to 5;

m is 0 or 1;

r is 0 to 3;

A is pyridinyl;

R<sup>1</sup> is (1) hydroxy, (2) oxo, (3) halogen, (4) cyano, (5) NR<sup>8</sup>R<sup>8</sup>, (6) SR<sup>8</sup>, (7) trifluoromethyl, (8) C<sub>1</sub>-C<sub>10</sub> alkyl, (9) OR<sup>8</sup>, (10) SO<sub>2</sub>R<sup>9</sup>, (11) OCOR<sup>9</sup>, (12) NR<sup>8</sup>COR<sup>9</sup>, (13) COR<sup>9</sup>, (14) NR<sup>8</sup>SO<sub>2</sub>R<sup>9</sup>, (15) NR<sup>8</sup>CO<sub>2</sub>R<sup>8</sup>, or (16) C<sub>1</sub>-C<sub>10</sub> alkyl substituted by hydroxy, halogen, cyano, NR<sup>8</sup>R<sup>8</sup>, SR<sup>8</sup>, trifluoromethyl, OR<sup>8</sup>, C<sub>3</sub>-C<sub>8</sub> cycloalkyl, phenyl, NR<sup>8</sup>COR<sup>9</sup>, COR<sup>9</sup>, SO<sub>2</sub>R<sup>9</sup>, OCOR<sup>9</sup>, NR<sup>8</sup>SO<sub>2</sub>R<sup>9</sup> or NR<sup>8</sup>CO<sub>2</sub>R<sup>8</sup>;

R<sup>2</sup> and R<sup>3</sup> are independently (1) hydrogen, (2) C<sub>1</sub>-C<sub>10</sub> alkyl or (3) C<sub>1</sub>-C<sub>10</sub> alkyl with 1 to 4 substituents selected from hydroxy, C<sub>1</sub>-C<sub>10</sub> alkoxy, or halogen;

X is (1) -CH<sub>2</sub>-, (2) -CH<sub>2</sub>-CH<sub>2</sub>-, (3) -CH=CH- or (4) -CH<sub>2</sub>O-;

R<sup>4</sup> and R<sup>5</sup> are independently (1) hydrogen, (2) C<sub>1</sub>-C<sub>10</sub> alkyl, (3) halogen, (4) NHR<sup>8</sup>, (5) OR<sup>8</sup>, (6) SO<sub>2</sub>R<sup>9</sup> or (7) NHSO<sub>2</sub>R<sup>9</sup>;

R<sup>6</sup> is (1) hydrogen or (2) C<sub>1</sub>-C<sub>10</sub> alkyl;

R<sup>7</sup> is Z-(R<sup>1a</sup>)<sub>n</sub>;

R<sup>1a</sup> is (1) R<sup>1</sup>, (2) C<sub>3</sub>-C<sub>8</sub> cycloalkyl, (3) phenyl optionally substituted with up to 4 groups independently selected from R<sup>8</sup>, NR<sup>8</sup>R<sup>8</sup>, OR<sup>8</sup>, SR<sup>8</sup> or halogen, or (4) 5 or 6-membered heterocycle with from 1 to 4 heteroatoms selected from oxygen, sulfur or nitrogen, optionally substituted with up to four groups independently selected from oxo, R<sup>8</sup>, NR<sup>8</sup>R<sup>8</sup>, OR<sup>8</sup>, SR<sup>8</sup>, or halogen;

Z is (1) phenyl, (2) naphthyl, (3) or a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur or nitrogen, (4) a benzene ring fused to a C<sub>3</sub>-C<sub>8</sub> cycloalkyl ring, (5) a benzene ring fused to a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur or nitrogen, (6) a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur or nitrogen fused to a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur or nitrogen, or (7) a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur or nitrogen fused to a C<sub>3</sub>-C<sub>8</sub> cycloalkyl ring;

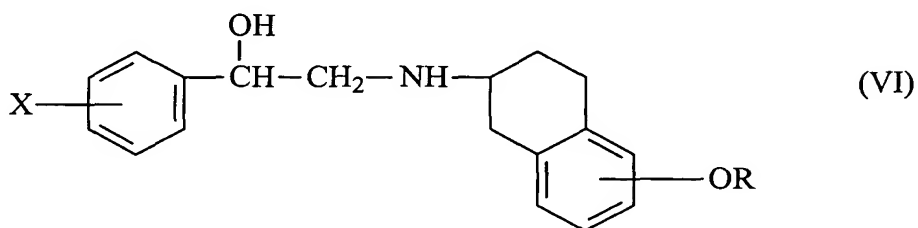
R<sup>8</sup> is (1) hydrogen, (2) C<sub>1</sub>-C<sub>10</sub> alkyl, (3) C<sub>3</sub>-C<sub>8</sub> cycloalkyl, (4) Z optionally having 1 to 4 substituents selected from halogen, nitro, oxo, NR<sup>10</sup>R<sup>10</sup>, C<sub>1</sub>-C<sub>10</sub> alkyl, C<sub>1</sub>-C<sub>10</sub> alkoxy, C<sub>1</sub>-C<sub>10</sub> alkylthio, and C<sub>1</sub>-C<sub>10</sub> alkyl having 1 to 4 substituents selected from hydroxy, halogen, CO<sub>2</sub>H, CO<sub>2</sub>-C<sub>1</sub>-C<sub>10</sub> alkyl, SO<sub>2</sub>-C<sub>1</sub>-C<sub>10</sub> alkyl, C<sub>3</sub>-C<sub>8</sub> cycloalkyl, C<sub>1</sub>-C<sub>10</sub> alkoxy, or Z optionally

substituted by from 1 to 3 halogen, C<sub>1</sub>-C<sub>10</sub> alkyl or C<sub>1</sub>-C<sub>10</sub> alkoxy, or (5) C<sub>1</sub>-C<sub>10</sub> alkyl having 1 to 4 substituents selected from hydroxy, halogen, CO<sub>2</sub>H, CO<sub>2</sub>-C<sub>1</sub>-C<sub>10</sub> alkyl, SO<sub>2</sub>-C<sub>1</sub>-C<sub>10</sub> alkyl, C<sub>3</sub>-C<sub>8</sub> cycloalkyl, C<sub>1</sub>-C<sub>10</sub> alkoxy, C<sub>1</sub>-C<sub>10</sub> alkyl, or Z optionally substituted by from 1 to 4 halogen, C<sub>1</sub>-C<sub>10</sub> alkyl or C<sub>1</sub>-C<sub>10</sub> alkoxy;

R<sup>9</sup> is (1) R<sup>8</sup> or (2) NR<sup>8</sup>R<sup>8</sup>; and

R<sup>10</sup> is (1) C<sub>1</sub>-C<sub>10</sub> alkyl, or (2) two R<sup>10</sup> groups together with the N to which they are attached forming a 5 or 6-membered ring optionally substituted with C<sub>1</sub>-C<sub>10</sub> alkyl;

(c) a compound of formula (VI) is:

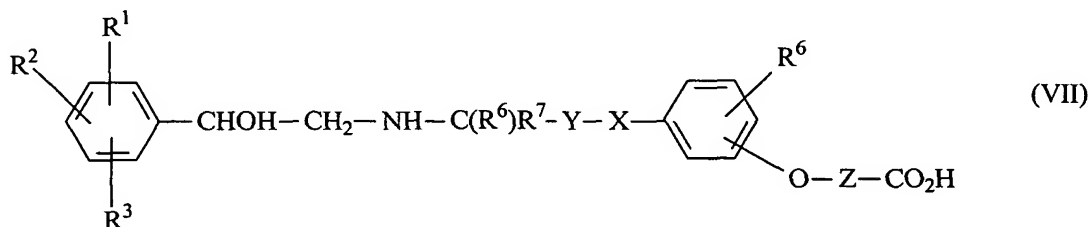


wherein

X is hydrogen, halogen, trifluoromethyl or lower alkyl, and

R is hydrogen; lower alkyl which may have a suitable substituent selected from the group consisting of cyclo(C<sub>3</sub>-C<sub>7</sub>)alkyl, hydroxy, lower alkoxy, carboxy and lower alkoxy carbonyl; cyclo(C<sub>3</sub>-C<sub>7</sub>)alkyl or lower alkanoyl;

(d) a compound of formula (VII) is represented by the following general formula:



wherein

R<sup>1</sup> is a hydrogen, fluorine, chlorine or bromine atom or a hydroxyl, hydroxymethyl, methyl, methoxyl, amino, formamido, acetamido, methylsulphonylamido, nitro, benzyloxy, methylsulphonylmethyl, ureido, trifluoromethyl or p-methoxybenzylamino group;

R<sup>2</sup> is a hydrogen, fluorine, chlorine or bromine atom or a hydroxyl group;



R<sup>3</sup> is a hydrogen, chlorine or bromine atom or a hydroxyl group,

R<sup>4</sup> is a hydrogen atom or a methyl group;

R<sup>5</sup> is a hydrogen atom or a methyl group;

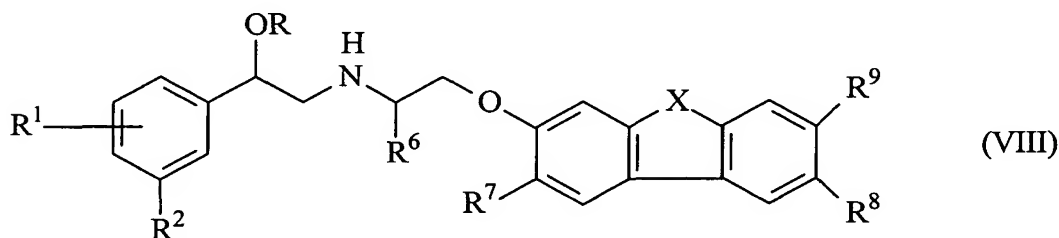
R<sup>6</sup> is a hydrogen, fluorine or chlorine atom or a methyl, methoxyl or hydroxy group;

X is an oxygen atom or a bond;

Y is an alkylene group of up to 6 carbon atoms or a bond; and

Z is an alkylene, alkenylene or alkynylene group of up to 10 carbon atoms; and

(e) a compound of formula (VIII) is represented by the following general formula:



wherein

R is hydrogen or methyl,

R<sup>1</sup> is hydrogen, halogen, hydroxy, benzyloxy, amino or hydroxymethyl,

R<sup>2</sup> is hydrogen, hydroxymethyl, -NHR<sup>3</sup>, -SO<sub>2</sub>NR<sup>4</sup>R<sup>4'</sup> or nitro,

R<sup>3</sup> is hydrogen, methyl, -SO<sub>2</sub>R<sup>5</sup>, formyl or -CONHR<sup>6'</sup>,

R<sup>4</sup> and R<sup>4'</sup> are independently hydrogen, lower alkyl or benzyl,

R<sup>5</sup> is lower alkyl, benzyl or -NR<sup>4</sup>R<sup>4'</sup>,

R<sup>6</sup> is hydrogen or lower alkyl,

R<sup>6'</sup> is hydrogen or lower alkyl,

R<sup>9</sup> is hydrogen, amino, acetylamino or hydroxy, and

X is N, O, S or methylene;

provided that when X is N, O or S,

then R<sup>9</sup> is hydrogen, either R<sup>7</sup> or R<sup>8</sup> is hydrogen, and the other is hydrogen, amino, acetylamino or hydroxy; and

provided that when X is methylene,

then both R<sup>7</sup> and R<sup>8</sup> are hydrogen

wherein said packaging material comprises a label or a written material which indicates that [the compound defined in Claim 10] said compound can or should be used for

preventing and/or treating dysuria.--